

ONE HUNDRED FIFTEENTH CONGRESS  
**Congress of the United States**  
**House of Representatives**  
COMMITTEE ON ENERGY AND COMMERCE  
2125 RAYBURN HOUSE OFFICE BUILDING  
WASHINGTON, DC 20515-6115

Majority (202) 225-2927  
Minority (202) 225-3641

**MEMORANDUM**

**October 1, 2017**

**To: Subcommittee on Health Democratic Members and Staff**  
**Fr: Committee on Energy and Commerce Democratic Staff**  
**Re: Hearing on “Examining Patient Access to Investigational Drugs”**

On **Tuesday, October 3<sup>rd</sup>, at 10:15 a.m., in Room 2322 of the Rayburn House Office Building**, the Subcommittee on Health will hold a hearing titled “Examining Patient Access to Investigational Drugs.”

**I. BACKGROUND**

Expanded access, also referred to as compassionate use, allows patients to gain access to investigational drugs, biologics and medical devices, outside of a clinical trial setting, that have not yet been approved by the Food and Drug Administration (FDA). The purpose of expanded access is to treat patients with serious or life-threatening diseases or conditions who have no other acceptable medical options and are ineligible for a clinical trial.

**II. FDA REQUIREMENTS FOR ALL EXPANDED ACCESS USES**

FDA has a long history of facilitating access to investigational therapies for seriously ill patients who have no comparable or satisfactory treatment alternatives. In 1987, regulations for investigational new drugs (INDs) were changed to provide access for a broader patient population under a treatment IND or protocol.<sup>1</sup>

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<sup>1</sup> Food and Drug Administration (FDA), *Expanded Access Programs* ([www.fda.gov/downloads/ForPatients/About/UCM410182.pdf](http://www.fda.gov/downloads/ForPatients/About/UCM410182.pdf)).

The 1997 FDA Modernization Act amended the Federal Food, Drug, and Cosmetic Act (FD&C) to allow individuals to obtain investigational products for diagnosis, monitoring, or treatment use when the following requirements are met:<sup>2</sup>

- The patient and his or her physician must both be willing participants. The physician must also determine that the patient has no comparable or satisfactory alternative therapy and that the risk from the investigational product is not greater than the probable risk from the disease or condition;
- FDA determines that there is sufficient evidence of safety and effectiveness to support use of the investigational drug in the particular circumstance;
- FDA determines that providing the investigational drug will not interfere with the initiation, conduct, or completion of clinical investigations to support marketing approval;
- The sponsor or clinical investigator (or the patient's physician in the case of a single patient expanded access request) submits a clinical protocol (a document that describes the treatment plan for the patient) sufficient to satisfy the requirements for INDs or investigational device exemptions (IDEs).
- The patient is unable to obtain the investigational drug under another IND or protocol, or to participate in a clinical trial.

### **III. EXPANDED ACCESS TO INVESTIGATIONAL DRUGS AND BIOLOGICS**

#### **A. Federal Regulation of Investigational New Drugs**

In 2009, FDA revised its IND regulations to establish three categories of expanded access for investigational drugs and biologics and to streamline the regulatory processes for Expanded Access programs. The three established categories are: (1) expanded access for individual patients, including for emergency use; (2) expanded access for intermediate-size patient populations; and (3) expanded access for widespread use through a treatment IND or treatment protocol.<sup>3</sup>

For each category of expanded access, a request can be submitted through either (1) an expanded access IND – which is a new IND submission that is separate and distinct from

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<sup>2</sup> FDA, *Expanded Access (Compassionate Use)* ([www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm#Statutory\\_Background](http://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm#Statutory_Background)).

<sup>3</sup> Subpart 1 of 21 CFR Part 312.

existing INDs and only intended for treatment use, or (2) as an expanded access protocol, submitted as a protocol amendment to an existing IND.<sup>4</sup>

FDA generally encourages requests to be submitted as an expanded access protocol, rather than a new expanded access IND, as it allows all expanded access use and clinical trial use to be consolidated under a single IND. Doing so may help facilitate identification of safety concerns, simplify the administrative process, and benefit product review.<sup>5</sup>

Under current law, FDA cannot require a pharmaceutical company to provide an unapproved drug to patients. The availability of an investigational product through expanded access is dependent on the agreement of the pharmaceutical company to make the drug available. Investigational products are made available to patients through either the company's own expanded access program or provided directly to the individual's physician for administration. FDA can only act on a request after a pharmaceutical company agrees to provide the drug through expanded access. A company may choose to deny an expanded access request for a variety of reasons. For example, a company may choose not to offer the drug because there is not enough of the drug available or there are concerns about adverse events in patients not participating in a trial that might influence FDA's review of the product.<sup>6</sup>

FDA approves nearly all of the expanded access requests for investigational drugs or biologics that they receive. In fact, for the past 5 years FDA's approval rate for expanded access requests has been over 99 percent.<sup>7</sup> For example, from October 1, 2015 to September 30, 2016, the FDA received a total of 1,554 requests for expanded access INDs and protocols and ultimately allowed 1,545 of those requests to proceed; an approval rate of 99.4 percent.<sup>8</sup>

In some instances, a patient may have to pay for the investigational drug. The pharmaceutical company may elect not to charge for the product or it may request authorization from FDA to charge for the direct and indirect costs of making the product available through

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<sup>4</sup> FDA, *Expanded Access to Investigational Drugs for Treatment Use—Qs & As, Guidance for Industry* (June 2016) ([www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm351261.pdf](http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm351261.pdf)).

<sup>5</sup> *Id.*

<sup>6</sup> National Organization for Rare Diseases (NORD), *Expanded Access FAQ* ([rarediseases.org/wp-content/uploads/2016/08/NORD-Expanded-Access-FAQ\\_Aug2016.pdf](http://rarediseases.org/wp-content/uploads/2016/08/NORD-Expanded-Access-FAQ_Aug2016.pdf)).

<sup>7</sup> FDA, *Expanded Access INDs and Protocols* ([www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/INDActivityReports/ucm373560.htm](http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/INDActivityReports/ucm373560.htm)).

<sup>8</sup> FDA, *Expanded Access Submission Receipts Report, Oct 1, 2015 - Sep 30, 2016* (<https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/INDActivityReports/UCM546129.pdf>).

expanded access. Investigational treatments are generally high cost and the majority of insurance companies will not cover access to an investigational drug.<sup>9</sup>

## **B. Expanded Access for Individual Patients**

In June 2016, FDA released final guidance for industry titled “Expanded Access to Investigational Drugs for Treatment Use—Qs & As.”<sup>10</sup> This guidance outlines what expanded access is, when and how expanded access can be requested, and the type of information that must be included in an expanded access request. The agency also released additional guidance establishing a new streamlined form, FDA 3926, which physicians can use to enroll patients into expanded access programs.<sup>11</sup> The streamlined 3926 form significantly reduced the time it takes to complete an expanded access application, it is estimated that the form takes 45 minutes to complete.<sup>12</sup>

In an emergency situation, in which there is no time to submit either form, treatment use for a single patient can be requested and authorized by telephone (or other rapid means of communication) and may start immediately upon FDA authorization. FDA physicians are available on a 24 hour basis to facilitate a prompt authorization when it is needed. FDA has noted that emergency requests are usually granted immediately over the phone, and non-emergencies are granted in a median of four days.<sup>13</sup>

## **IV. LEGISLATION**

### **A. States ‘Right to Try’ Legislation**

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<sup>9</sup> FDA, *Expanded Access: Information for Patients* (www.fda.gov/ForPatients/Other/ExpandedAccess/ucm20041768.htm).

<sup>10</sup> FDA, *Expanded Access to Investigational Drugs for Treatment Use—Qs & As, Guidance for Industry* (June 2016) (www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm351261.pdf).

<sup>11</sup> FDA, *Individual Patient Expanded Access Applications: Form FDA 3926, Guidance for Industry* (June 2016) (https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM432717.pdf).

<sup>12</sup> *Id.*

<sup>13</sup> FDA, Dr. Peter Lurie, Testimony before Senate Homeland Security and Governmental Affairs Committee (Sept. 22, 2016).

To date 37 states and the District of Columbia have passed ‘Right to Try’ laws.<sup>14</sup> Though each law varies, they generally allow for a terminally ill patient to gain access to investigational products that have only passed a Phase 1 clinical trial without FDA approval. Phase 1 clinical trials are the first studies in humans (in the range of 20 to 80 patients) and are used to determine the toxicity of a drug product; these studies do not examine efficacy, safety, or side effects. States’ right to try laws do not compel insurers to cover the costs of the experimental therapies.<sup>15</sup>

**B. S. 204, Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017**

On August 3, 2017, S. 204 passed the Senate. This legislation would establish a separate pathway for patients with life-threatening diseases, which is broadly defined to include patients with chronic conditions such as diabetes or HIV, without any FDA review or approval. Investigational drugs that have completed a Phase 1 clinical trial would be eligible for expanded access. FDA would be unable to use any clinical outcomes associated with the use of the investigational treatments unless the manufacturer requests the use of the outcomes, or if FDA justifies that the outcome would be critical to determining the safety of the investigational product. A manufacturer, prescriber, dispenser, or any other individual entity would have no liability regarding the treatment unless their conduct amounts to reckless or willful misconduct, gross negligence or intentional tort under state law.

**C. H.R. 2430, the FDA Reauthorization Act of 2017**

The FDA Reauthorization Act of 2017, which was signed into law on August 18, 2017, included provisions intended to address some of the potential barriers patients have relating to access to investigational treatments. Section 610 requires FDA to conduct a public meeting on clinical trial inclusion and exclusion criteria, and to issue a report about barriers to patients participating in clinical trials and potential solutions to include additional populations. FDA is required to issue guidance to manufacturers for how to expand clinical trials to broader populations and improve access to treatments for people who do not qualify for clinical trials. FDA must also issue guidance or regulations to streamline the institutional review board review for individual patient expanded access protocols. Manufacturers of a drug that has been designated as a breakthrough therapy, fast track product, or regenerative advanced therapy would also now be subject to the requirement to publish its expanded access policy. Finally, it requires GAO to report on individual access to investigational drugs through the Expanded Access program.

**D. The 21st Century Cures Act**

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<sup>14</sup> National Conference of State Legislatures, “*Right to Try*” *Experimental Prescription Medicines State Laws and Legislation for 2014 -2017* ([http://www.ncsl.org/research/health/state-laws-and-legislation-related-to-biologic-medications-and-substitution-of-biosimilars.aspx#Right\\_to\\_Try](http://www.ncsl.org/research/health/state-laws-and-legislation-related-to-biologic-medications-and-substitution-of-biosimilars.aspx#Right_to_Try)).

<sup>15</sup> Elizabeth Richardson et al., *Health Policy Brief: Right to Try Laws*, Health Affairs (March 5, 2015) ([healthaffairs.org/healthpolicybriefs/brief\\_pdfs/healthpolicybrief\\_135.pdf](http://healthaffairs.org/healthpolicybriefs/brief_pdfs/healthpolicybrief_135.pdf)).

The 21<sup>st</sup> Century Cures Act, which was signed into law on December 13, 2016, included changes to expanded access policies. Section 3032 requires certain manufacturers or distributors of investigational drugs to make information regarding their expanded access policy publicly available. It does not, however, compel a manufacturer or distributor to offer a product through an expanded access program.

**V. WITNESSES**

**Panel One:**

**Representative Andy Biggs (R-AZ)**  
**Representative Brian Fitzpatrick (R-PA)**

**Panel Two:**

**Scott Gottlieb, M.D.**  
Commissioner  
U.S. Food and Drug Administration

**Panel Three:**

**John Dicken**  
Director, Health Care  
U.S. Government Accountability Office (GAO)

**Panel Four:**

**Naomi Lopez-Bauman**  
Director of Healthcare Policy  
Goldwater Institute

**Lieutenant Commander Matthew Bellina**  
U.S. Navy (Retired)

**Kenneth I. Moch**  
President and CEO  
Cognition Therapeutics, Inc.

**Alison Bateman-House, PhD, MPH, MA**  
Assistant Professor  
Department of Population Health, New York University (NYU) Langone Health

**Ellen V. Sigal**  
Chairperson and Founder  
Friends of Cancer Research